

What is claimed is:

1. An isolated ESM-1 polypeptide comprising an amino acid sequence selected from the group consisting of:

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(a) an amino acid sequence comprising a sequence of SEQ ID NO:2 ;

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(b) a variant of an amino acid sequence comprising a sequence of SEQ ID NO:2, wherein one or more amino acid residues in said variant differs from the amino acid sequence of said mature form, provided that said variant differs in no more than about 30% of amino acid residues from said amino acid sequence;

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(c) a secreted mature form of an amino acid sequence of SEQ ID NO:19;

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(d) a variant of a mature form of an amino acid sequence of SEQ ID NO:19, wherein one or more amino acid residues in said variant differs from the amino acid sequence of said mature form, provided that said variant differs in no more than about 30%, of the amino acid residues from the amino acid sequence of said mature form; and

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(e) a fragment of the amino acid sequence of SEQ ID NO:2, or SEQ ID NO:19.

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2. The ESM-1 polypeptide of claim 1, wherein said polypeptide comprises an amino acid sequence of a naturally-occurring allelic variant of an amino acid sequence selected from the group consisting of SEQ ID NO:2, and SEQ ID NO:3.

3. The polypeptide of claim 1, wherein the amino acid sequence of said variant comprises a conservative amino acid substitution.

5 4. An isolated ESM-1 polypeptide comprising an amino acid sequence selected from the group consisting of: SEQ ID NO:2, or SEQ ID NO:3.

10 5. An isolated nucleic acid molecule comprising a nucleic acid sequence encoding the polypeptide of claim 1.

6. The isolated nucleic acid molecule of claim 1 wherein the nucleic acid sequence comprises a sequence selected from the group consisting of:

15 a) a nucleic acid sequence capable of hybridizing under stringent conditions , or which would be capable of hybridizing under said conditions but for the degeneracy of the genetic code , to the DNA sequence of SEQ ID NO:1;

20 b) a nucleic acid sequence having at least about 80% homology to the DNA sequence of SEQ ID NO:1; and

25 c) a complement of SEQ IDNO:1.

7. The nucleic acid molecule of claim 6, wherein the nucleic acid molecule is SEQ ID NO:1.

30 8. The nucleic acid molecule of claim 6, wherein said nucleic acid molecule hybridizes under stringent conditions to a nucleotide sequence of SEQ ID NO:1 or a complement of said nucleotide sequence.

9. A vector comprising the nucleic acid molecule of claim 5, 6, 7, or 8.

5 10. The vector of claim 9, further comprising a promoter operably linked to said nucleic acid molecule.

11. A host cell comprising the vector of claim 10.

10 12. A method of producing an ESM-1 polypeptide comprising: growing under suitable nutrient conditions, a host cell of claim 11 under conditions that result in the expression of said ESM-1 polypeptide.

15 13. A microarray comprising the nucleic acid sequence of claim 1.

14. The microarray of claim 13 wherein said nucleic acid sequence comprises the nucleic acid sequence of SEQ ID NO:1.

20 15. An antibody that immunospecifically-binds to the ESM-1 polypeptide of claim 1.

25 16. The antibody of claim 15, wherein said antibody is a monoclonal antibody.

17. The antibody of claim 16, wherein said antibody is an antibody fragment.

30 18. The antibody of claim 17, wherein said antibody fragment is selected from the group consisting of a Fv fragment, a Fab fragment, (Fab)<sub>2</sub> fragment, and a single chain antibody.

19. The antibody of claim 15, 16, 17, or 18, wherein said antibody is an antagonist.

5 20. The antibody of claim 19 wherein the antibody is a humanized antibody.

21. The antibody of claim 19 wherein the antibody is a fully human antibody.

10 22. A method of identifying an agent that binds to the ESM-1 polypeptide of claim 1, the method comprising:

(a) contacting said polypeptide with said agent; and

(b) determining whether said agent binds to said polypeptide.

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23. A method for identifying an agent that modulates the expression or activity of the ESM-1 polypeptide of claim 1, the method comprising:

20 (a) providing a cell expressing said polypeptide in an operational manner;

(b) contacting the cell with said agent; and

25 (c) determining whether the agent modulates expression or activity of said polypeptide,

whereby an alteration in expression or activity of said peptide indicates said agent modulates expression or activity of said polypeptide.

30 24. A method for modulating the activity of the ESM-1 polypeptide of claim 1, the method comprising: contacting a cell sample expressing the ESM-1 polypeptide of claim 1 with a compound that binds to said polypeptide in an amount sufficient to modulate the activity of the polypeptide.

25. A method of treating or preventing an angiogenesis associated disorder, said method comprising administering to a subject in which such treatment or prevention is desired the ESM-1 polypeptide of claim 1 in an amount sufficient to treat or prevent said angiogenesis associated disorder in said subject.

26. A method of treating or preventing an angiogenesis associated disorder, said method comprising administering to a subject in which such treatment or prevention is desired the antibody of claim 19 in an amount sufficient to treat or prevent said angiogenesis associated disorder in said subject.

27. A pharmaceutical composition comprising the ESM-1 polypeptide of claim 1 and a pharmaceutically acceptable carrier.

28. A pharmaceutical composition comprising the antibody of claim 19 and a pharmaceutically acceptable carrier.

29. A kit comprising the pharmaceutical composition of claim 28.

30. A method of detecting differentially expressed genes correlated with a cancerous state of a mammalian cell, the method comprising the step of detecting at least one differentially expressed gene product in a test sample derived from a cell suspected of being cancerous, where the gene product is encoded by the nucleic acid sequence SEQ ID NO:1, wherein detection of differentially expressed product is correlated with a cancerous state of the cell from which the test sample was derived.

31. A method for detecting the presence of a nucleic acid molecule of claim 6 in a sample comprising:

a) contacting the sample with a nucleic acid probe or primer which selectively hybridizes to the nucleic acid molecule; and

5                   b) determining whether the nucleic acid probe or primer binds to a nucleic acid molecule in the sample to thereby detect the presence of a nucleic acid molecule of claim I in the sample.

32.     A method for monitoring the progression of an angiogenic disorder in a patient, the method comprising:

10                   a) detecting in a patient sample at a first point in time, the expression of a marker, wherein the marker is the ESM-1 polypeptide of claim 1;

15                   b) repeating step a) at a subsequent point in time; and

c) comparing the level of expression detected in steps a) and b), and therefrom monitoring the progression of the angiogenic disorder.

20                   33.     A method of assessing the efficacy of a test compound for inhibiting angiogenesis, the method comprising comparing:

a) expression of a marker in a first sample obtained from a patient exposed to the test compound, wherein the marker is the ESM-1 polypeptide of claim 1, and

25                   b) expression of the marker in a second sample obtained from the patient, wherein the sample is not exposed to the test compound, wherein a significantly lower level of expression of the marker in the first sample, relative to the second sample, is an indication that the test compound is efficacious for inhibiting the cancer in the patient.

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34.     A method of assessing the efficacy of a therapy for inhibiting angiogenesis in a patient, the method comprising comparing:

a) expression of a marker in the first sample obtained from the patient prior to providing at least a portion of the therapy to the patient, wherein the marker is ESM-1 polypeptide of claim 1, and

5                   b) expression of the marker in a second sample obtained from the patient following provision of the portion of the therapy, wherein a significantly lower level of expression of the marker in the second sample, relative to the first sample, is an indication that the therapy is efficacious for inhibiting the cancer in the patient.

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35.       A method of selecting a composition for inhibiting angiogenesis in a patient, the method comprising:

15                   (a)     obtaining a sample comprising cancer cells from the patient;

                 (b)     separately exposing aliquots of the sample in the presence of a plurality of test compositions;

20                   (c)     comparing expression of a marker in each of the aliquots, wherein the marker is selected from the group consisting of the markers of SEQ ID NO:2, and SEQ ID NO:3, and

25                   (d) selecting one of the test compositions which alters the level of expression of the marker in the aliquot containing that test composition, relative to other test compositions.

36.       An ESM-1 polypeptide antagonist.

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37.       The antagonist of claim 36 wherein said antagonist is an antisense molecule.

38. A chimeric molecule comprising the ESM-1 polypeptide of claim 1.

5 39. A transgenic non-human mammal having integrated into its genome a nucleic acid sequence encoding ESM-1 operatively linked to regulatory elements, wherein expression of said coding sequence increases the level of ESM-1 relative to a non-transgenic mammal of the same species, wherein the coding sequence is the nucleic acid of claim 6.

10 40. The mammal of claim 39, which is a mouse.

41. A transgenic knockout non-human mammal comprising a homozygous disruption in its endogenous ESM-1 gene, wherein said disruption prevents the expression of a functional ESM-1 protein.